

REMARKS

Claims 1, 3-11, 13, 15-31, 37, 38, 40-47 and 56-67, as amended, are pending in this application for the Examiner's review and consideration. Claims 11, 27, 30 and 46 have been amended to correct informalities as suggested by the Examiner. Claims 1, 37 and 59 were amended to recite that the permeation enhancer is a monoalkyl ether of diethylene glycol or a tetraglycol furol. Also, claims 37 and 59 were amended to recite that the alkanol is present in an amount between about 5 to 80% by weight of the delivery vehicle, the polyalcohol is present in an amount between about 1% to 15% by weight of the delivery vehicle, and the permeation enhancer is present in an amount between about 0.2% to 15% by weight of the delivery vehicle. These features were previously presented in other claims and in the specification as originally filed. Since no new matter has been introduced by these changes, they all should be entered at this time.

Claims 11, 27 and 30 have been objected to for informalities. In response, claims 11, 27 and 30 have been amended to correct these informalities. Therefore, the objection has been overcome and should be withdrawn.

Claims 1, 5-7, 11 and 64 have been rejected under 35 U.S.C. 102(b) as being anticipated by International Patent Application Publication No. WO 2002/011768 to Carrara et al. (referred to hereafter as "Carrara"). Carrara relates to a pharmaceutical formulation with good cosmetic properties and low irritation potential for the systemic treatment of diverse diseases by transdermal or transmucosal route, comprising as permeation enhancers defined amounts of fatty alcohols such as lauryl alcohol, n-decanol and oleyl alcohol in a ternary vehicle composite consisting of ethanol, propylene glycol and water, and optionally also a monoalkylether of diethylene glycol.

Claim 1 recites that the composition of the present invention is substantially free of long-chain fatty alcohols, long-chain fatty acids and long-chain fatty esters to avoid undesirable odor and irritation from such compounds during use of the formulation. In contrast, the formulation of Carrara is characterized by its inclusion of long chain fatty alcohols. In fact, by expressly including these compounds, Carrara teaches away from the exclusion of long chain fatty alcohols. In particular, to emphasize the importance of the presence of long chain fatty alcohols, Carrara presents side-by-side comparisons of formulations with and without these compounds as shown in Tables VII and VIII of Carrara. Specifically, a formulation containing both lauryl

alcohol (a long chain fatty alcohol) and diethylene glycol monoethyl ether (Example 1) has an intro flux rate three times of that of a formulation containing diethylene glycol monoethyl ether alone (Example 2). In contrast, a formulation containing lauryl alcohol alone (Example 3) has an intro flux rate only slightly lower than that of the formulation containing both lauryl alcohol and diethylene glycol monoethyl ether (Example 1). Thus, long-chain alcohols are indispensable components of the permeation enhancer formulation of Carrara.

Moreover, Carrara specifically refers to his formulations, which contain long-chain alcohols, as having low irritation potentials and good cosmetic properties, but Carrara does not provide any motivation to exclude these compounds to avoid undesirable characteristics such as undesirable odors. Thus, Carrara does not disclose the presently claimed invention.

Furthermore, the present formulation uses different amounts of the components than what is disclosed in Carrara, and the new delivery vehicle of the present claims utilizes balanced amounts to provide the desired permeation enhancement. In Carrara, the delivery vehicle includes a C2-C4 alkanol such as ethanol, isopropanol, n-propanol, or butanol present in an amount of about 5 to about 75 % w/w; and a polyalcohol or glycol such as propylene glycol, butylene glycol, hexylene glycol, or ethylene glycol present in an amount of about 0.5 to about 50 % w/w. A permeation enhancer of a saturated fatty alcohol or fatty acid is present in an amount of about 0.1 to about 20 % w/w and, optionally, a diethylene glycol monoalkyl ether can be present in an amount of up to 40.0 % w/w. In contrast, in the present invention, the alkanol is present in an amount between about 5 to 80%, and in some embodiments 25 to 65%, by weight of the delivery vehicle, and the polyalcohol is present in an amount between about 1% to 15% by weight of the delivery vehicle. Also, the permeation enhancer is a monoalkyl ether of diethylene glycol or a tetraglycol furol, and is present in an amount between about 0.2% to 15% by weight of the delivery vehicle. Additionally, in some embodiments, as defined by claims 6 and 41, the polyalcohol and permeation enhancer are present in a total amount of 15% by weight. Such optimizing of amounts and ratios of different components is not routine for a skilled artisan, and to arrive at the presently claimed components and amounts requires significant amount of research and investigation, which, of course, is the work of the present inventors and not that of the prior art. Furthermore, no fatty alcohol or fatty acid is present in the presently claimed formulation. Thus, the presently claimed formulation avoids undesirable odor and irritation from such fatty compounds during use of the formulation and the delivery vehicle facilitates

irritation from such fatty compounds during use of the formulation and the delivery vehicle facilitates absorption of the at least one active agent by the dermal or mucosal surfaces so that transfer or removal of the formulation from such surfaces is minimized. Therefore, the rejection based on Carrara should be withdrawn.

Claims 1, 5, 6, 8-11, 13, 15-28, 37, 38, 40-47, 56-58 and 61-65 have been rejected under 35 U.S.C. 103(a) as unpatentable over US Patent No. 6,319,913 to Mak et al. (referred to hereafter as "Mak") in view of US Patent No. 5, 397,771 to Bechgaard et al. (referred to hereafter as "Bechgaard").

Mak discloses a transdermal and topical drug composition capable of enhancing the penetration of transdermally or topically applied drugs with reduced skin irritation that often accompanies transdermal and topical drug delivery. The composition of Mak is different from that of the present invention. First of all, Mak requires a much higher amount of glycol, i.e. "about 25% to about 55% weight to weight of the composition"(col. 4, ll. 56-57 of Mak), in comparison with that of the present invention, i.e. about 1% to 15%. Moreover, as acknowledged by the Examiner, the composition of Mak uses oleic acid, a long chain fatty acid, which is specifically excluded from the composition of the present invention. As an attempt to remedy the deficiencies of Mak, Bechgaard was cited.

Applicants respectfully submit that Bechgaard does not remedy the deficiencies of Mak. Bechgaard discloses a pharmaceutical preparation comprising an n-glycofurol for application of an effective amount of one or more biologically active substance(s) to a mucosal membrane of a mammal, which produces a high plasma concentration of the pharmaceutically active substance(s) nearly as rapid as by i.v. administration. There is no teaching or suggestion in either reference to motivate a person of ordinary skill in the art to replace the oleic acid in the composition of Mak with the n-glycofurol taught by Bechgaard, as suggested by the Examiner. More importantly, Mak specifically teaches that oleic acid is far superior than other permeation enhancers, including those closely related compounds such as oleyl alcohol in its ability to reduce skin irritation (col. 4, ll. 28-30 of Mak). Thus, Mak teaches away from the present invention by mandating the presence of oleic acid. Therefore, a person of ordinary skill in the art, following the teachings of Mak, will not even choose to replace the oleic acid in the composition of Mak with closely related compounds, let alone unrelated permeation enhancers

such as the n-glycofurol taught by Bechgaard. Therefore, the rejection is improper and should be withdrawn.

Claims 1, 3-11, 13, 15-31, 37, 38, 40-47 and 56-67 have been rejected under 35 U.S.C. 103(a) as unpatentable over Mak in view of Bechgaard and further in view of US Patent No. 6,503,894 to Dudley et al. (referred to hereafter as "Dudley") in view of US Patent No. 5,955,455 to Labrie et al. (referred to hereafter as "Labrie").

As explained above, Mak and Bechgaard do not teach the present invention as claimed. Dudley and Labrie do not remedy the deficiencies of the primary references either. Dudley teaches a pharmaceutical composition useful for treating hypogonadism comprising an androgenic or anabolic steroid, a C1-C4 alcohol, a penetration enhancer such as isopropyl myristate, and water. Labrie teaches the treatment of vaginal atrophy, hypogonadism, diminished libido, loss of collagen or connective tissues in the skin using sex steroid precursors such as dehydroepiandrosterone and dehydroepiandrosterone sulphate. As explained above, Mak teaches away using permeation enhancers other than oleic acid. Thus, contrary to the Examiner's suggestion, a person of ordinary skill in the art, following the teachings of Mak, will not even choose to replace the oleic acid in the composition of Mak with closely related compounds, let alone other unrelated permeation enhancers as those taught by Bechgaard or Dudley. Therefore, the cited references do not render the present claims obvious. Thus, the rejection should be withdrawn.

Accordingly, it is believed that the entire application is now in condition for allowance, early notice of which would be appreciated. In the event that the Examiner does not agree that all claims are now allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues in an effort to expedite the eventual allowance of this application.

3/18/09

Date

Respectfully submitted,



Allan A. Fanucci

(Reg. No. 30,256)

WINSTON & STRAWN LLP

Customer No. 28765

212-294-3311